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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,426	03/10/2005	Yu Momose	10525.0008	7181

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EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
08/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,426	MOMOSE ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8-10,15-17,20 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,4-6,8-10,15-17,20 and 25* is/are allowed.

6)☒ Claim(s) *22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 4-6, 8-10, 15-17, 20 and 22-25 are pending in the instant application. Claims 2, 3, 7, 11-14, 18, 19, 21 26 and 28 were cancelled by amendment filed on July 18, 2007. Claims 27 and 29 were previously cancelled.

Response to Amendment

2. The amendment and arguments filed on July 18, 2007 were fully considered. All grounds of rejection/objection set forth in the previous office action were overcome by amendment. A new ground of rejection is set forth herein, see Section 4.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on March 10, 2005 was fully considered. An updated signed copy of form 1449 is enclosed herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 22-24 rejected under 35 U.S.C. 112, first paragraph because the specification does not properly provide enablement for making

a) retinoid-related receptor function regulating agent,

and for the intended use of b)-d) for the treatment of diseases *other than* diabetes mellitus, insulin resistance, obesity and for the prophylaxis of any of the claimed diseases (eg. diabetes mellitus, hyperlipidemia, impaired glucose tolerance, obesity).

b) retinoid-related receptor function regulating agent,

c) peroxisome proliferator-activated receptor ligand.

d) retinoid X receptor ligand.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims

a) The claims are drawn to retinoid-related receptor function regulating agent, that comprises the instantly claimed compounds. The term "retinoid-related receptor function regulating agent," is defined in the specification (p. 65):

> In addition, the term "retinoid-related receptor" used here is classified as a nuclear receptor, and is a DNA-binding transcription factor whose ligand is a signal molecule such as oil-soluble vitamins etc., and may be any of a monomer receptor, a homodimer receptor and a heterodimer receptor.

The claims encompass all receptors that belong to the "superfamily" which comprises, for example, retinoic acid receptor RARα, β and γ (Farmer et al., p. 2352 1st column).

b)-d) The claims are drawn to "agents" for the following intended (instant specification p. 67):

> The compound of the present invention can be used as, for example, an agent for the prophylaxis or treatment of diabetes mellitus (e.g., type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes mellitus, etc.); an agent for the prophylaxis or treatment of hyperlipidemia (e.g., hypertriglyceridemia, hypercholesterolemia, hypo-high-density-lipoproteinemia, postprandial hyperlipemia etc.); an agent for improving insulin resistance; an insulin sensitizer; an agent for the prophylaxis or treatment of impaired glucose tolerance (IGT); an agent for the prophylaxis or treatment of obesity; an agent for the prophylaxis or treatment of hypertension; and an agent for preventing progress from impaired glucose tolerance to diabetes mellitus.

The nature of the invention

a)-d) Compounds of formula (I) are disclosed to possess PPAR γ binding and PPAR γ antagonistic activities. Although additional disclosure is not provided, it is further stated in the specification (p. 66):

> The compound of the present invention has an excellent ligand activity, in particular to retinoid X receptors (RXRα, RXRβ, RXRγ) and to peroxisome proliferator-activated receptors (PPARα, PPARβ (PPARδ), PPARγ), among the above-mentioned retinoid-related receptors, and is useful as an agonist, a partial agonist, an antagonist or a partial antagonist.

The state of the prior art/level of ordinary skill/level of predictability

a) It is known in the art that the various receptors in the superfamily of "retinoid receptors" have distinct ligand binding and activation properties.

Thus, a ligand that binds and regulates RXRα/β/γ does not necessarily bind and/or regulate any other receptor in the family. See for example, Farmer et al. p. 2353 Table 1.

b)-d) Although an art recognized correlation exists between in vitro/vivo PPAR γ antagonism and the treatment of diabetes mellitus, insulin resistance, and obesity (Rieusset et al., abstract), such correlation does not extend beyond the scope of these diseases. For example, the art recognized treatment of hypertension does not involve the use of nuclear receptors (page 2, http://www.healthatoz.com/healthatoz/Atoz/common/standard/transform.jsp?requestURI=/healthatoz/Atoz/dc/cen/card/hypr/hypertreat.jsp).

Prophylaxis of Diseases: see exemplary discussion below

1. Diabetes Mellitus:
   It is known in the art that Type 2 diabetes is treated by a combination of weight reduction, diabetic diet, exercise and medication (http://www.medicinenet. com/diabetes_treatment/article.htm, page 1 of 3). Thus, even with the existence of a nexus between treatment and nuclear receptors, medication alone is not sufficient to prevent/cure the disease.

2. Obesity:
   The use of medication alone does not prevent obesity; the amount of calories burned must exceed the calories taken in (http://www.webmd.com/diet/tc/Obesity-Overview)

3. Other Diseases:
   Similar arguments as described above apply to the other diseases encompassed by the claims. That is, a correlation between the disclosed activity and prophylaxis of these diseases does not currently exist.

The amount of direction provided by the inventor/existence of working examples

a) The disclosure provides a method of preparing compounds of formula (I) that have PPAR γ antagonism and PPAR γ binding activity. It is also stated that the compounds have ligand activity towards other PPAR receptors as well as retinoid X receptors. There is no disclosure of activity of the instantly claimed compounds as agents for other nuclear receptors, for example, retinoic acid receptors.

The quantity of experimentation needed to make or use the invention

a) Based on the unpredictability in the art for regulating the superfamily of nuclear receptors, absent guidance one of ordinary skill is not enabled by the disclosure to make compounds that are, broadly,

retinoid-related receptor function regulating agent,. One of ordinary skill is not enabled to practice the invention commensurate in scope with the claims.

b)-d) In the absence of guidance and/or nexus between the disclosed activty and the treatment/prevention of the diseases encompassed by the claims, one of ordinary skill is not enabled by the instant disclosure to practice the invention commensurate in scope with the claims. One of ordinary skill is not enabled to practice the intended use for:
retinoid-related receptor function regulating agent,
peroxisome proliferator-activated receptor ligand, and retinoid X receptor ligand.

Conclusions

5. Claims 1, 4-6, 8-10, 15-17 and 20 allowed. Claims 22-24 rejected.

6. Any inquiry concerning this communication should be directed to Sun Jae Y. Loewe, Ph.D. whole telephone number is 571-272-9074. The examiner can normally be reached on Monday through Friday from 7:30 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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